

## REMARKS

### Introductory Comments:

Claims 21-30 were examined in the Office Action dated June 16, 2006.

Claims 21-30 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite.

Claims 21-22, 24, and 28 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by U.S. Patent No. 5,470,705 to Grossman et al. (Grossman).

Claims 21-25, and 27-29 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over U.S. Patent No. 6,027,890 to Ness et al. (Ness) in view of Grossman.

Claim 26 was rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Grossman.

Claim 30 was rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Grossman further in view of U.S. Patent No 6,331,530 to Breslow et al. (Breslow).

Claims 21-30 were provisionally rejected on the grounds of non-statutory obviousness-type double patenting over U.S. Application No. 10/779,255.

Claims 21-30 were provisionally rejected on the grounds of non-statutory obviousness-type double patenting over U.S. Patent No. 6,770,439.

Claims 21-30 were provisionally rejected on the grounds of non-statutory obviousness-type double patenting over U.S. Patent No. 7,001,725.

Claims 21-30 were provisionally rejected on the grounds of non-statutory obviousness-type double patenting over U.S. Patent No. 6,673,550.

## SUPPORT FOR AMENDMENTS

The applicants have amended the first paragraph of the specification to recite related application information.

Claim 26 has been amended to recite that from 5 to 100 different electrophoretic probes form distinct peaks. The amendment corrects for antecedent basis.

Claim 30 has been amended to not depend from itself. The amendment thus corrects for a minor error.

Accordingly, no new matter has been added by way of this amendment and the entry thereof is respectfully requested.

## Addressing the Examiner's Rejections

### Rejections of the Claims Under 35 U.S.C. §112, second paragraph

The Examiner rejected claims 21-30 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite.

1. The applicants traverse the rejection of the claims because the phrase “aggregation” is said to be vague. The specification, at paragraph 209, for example, provides a definition of the phrase “aggregation.” Thus, in view of the knowledge in the field and the disclosure, one of ordinary skill in the art would know what is encompassed by the phrase.

2. The applicants have amended claim 30 so that it does not depend on itself, and thank the Examiner for the suggestion.

3. The applicants have amended claim 26 so that it does not recite the phrase "said plurality" and thank the Examiner for suggesting that the antecedent basis should be corrected.

In view of the above remarks, the Examiner is respectfully requested to withdraw the rejection.

**Rejections of the Claims Under 35 U.S.C. §102(b)**

The Examiner rejected claims 21-22, 24, and 28 under 35 U.S.C. §102(b) as allegedly being anticipated by U.S. Patent No. 5,470,705 to Grossman et al. (Grossman).

The applicants traverse the rejection. In order for a reference to anticipate an invention, the reference must teach each and every element of the claimed invention. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379, 231 USPQ 81, 90 (Fed. Cir. 1986). *Atlas Powder Co. v. E. I. du Pont De Nemours & Co.*, 750 F.2d 1569, 1574, 224 USPQ 409, 411 (Fed. Cir. 1984). Moreover, the single source must disclose all of the claimed elements "arranged as in the claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236 9 USPQ 2d 1913, 1920 (Fed. Cir. 1989); *Connell v. Sears Roebuck & Co.*, 722 F.2d 1542, 1548, 220 USPQ 193, 198 (Fed. Cir. 1983). The cited reference does not disclose all the elements of the applicants' claims.

Claims 21-22, 24, and 28 pertain to electrophoretic probes that have a cleavable linkage L and, upon cleavage of L, an eTag reporter comprising a detection group D and a mobility modifier M is produced. Grossman does not disclose probes having a cleavable linkage L. The Grossman probes are disclosed in Figure 1 and discussed at column 6, line 56-column 8, line 28.

At column 6, line 66 to column 7, line 3, the reference states that the “[p]robe 20 includes an oligonucleotide binding polymer 22 which preferably includes at least 10-20 bases, for requisite basepair specificity, and has a base sequence which is complementary to region 24 in target polynucleotide 26, with such in single-stranded form.” At no point does Grossman disclose electrophoretic probes having a cleavable linkage L. The cited reference does not disclose all the elements of the claims, and therefore, does not anticipate the applicants’ invention.

Therefore, the Examiner is respectfully requested to withdraw the rejection.

#### **Rejections of the Claims Under 35 U.S.C. §103(a)**

(a) The Examiner rejected claims 21-25, and 27-29 under 35 U.S.C. §103(a) as allegedly being unpatentable over U.S. Patent No. 6,027,890 to Ness et al. (Ness) in view of Grossman.

In order for the Office to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references. Second, there must be a reasonable expectation of success. Finally, the prior art references must teach or suggest all the claim limitations. The teachings or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant’s disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). The cited references do not disclose all the elements of the applicants’ claims, therefore, a *prima facie* case of obviousness has not been made.

Ness discloses mass spectrometry tags (column 16, line 27 onwards), infrared tags (column 18, line 41 and onwards), UV tags (column 19, lines 10-29), fluorescent tags (column 19, lines 30-57), and potentiometric tags (column 19, line 58-column 29, line 17). The reference

does not disclose eTag reporters of different electrophoretic probes that form distinct peaks upon electrophoretic separation. As discussed above, Grossman does not disclose electrophoretic probes having a cleavable linkage L. Thus, the combination of Ness and Grossman does not disclose all the elements of the claims.

Further, the cited art does not teach or provide a motivation to combine the teachings. The motivation to combine is said to be provided the fact that the ratio of charge/translation frictional drag is distinctive for each probe and the electrophoretic movement can be resolved. These are generalized scientific goals that cannot substitute for the particularity needed to establish a *prima facie* case of obviousness. The Examiner must show “reasons that the skilled artisan, confronted with the same problem as the inventor, and with no knowledge of the claimed invention, would select the elements from the cited prior art reference for combination in the manner claimed.” *In re Rouffet*, 47 USPQ2d at 1458, 1453 (Fed. Cir. 1998). Thus, the motivation to combine must be particularized, and the required evidence cannot be substituted with a generalized scientific goal, as the Examiner has done in the present case. At no point do the combined references disclose or suggest that cleavage of L produces an eTag reporter comprising a detection group, D, and a mobility modifier, M, with a unique electrophoretic mobility so that eTag reporters of different electrophoretic probes form distinct peaks upon electrophoretic separation.

The particularity needed to establish a motivation to combine references was further discussed in *In re Lee*, 61 USPQ2d 1430 (Fed. Cir. 2002). In *In re Lee*, the Board had determined that it was not necessary to present a source of a teaching, suggestion, or motivation to combine the references because the conclusion of obviousness may be made from common knowledge and common sense of a person of ordinary skill in the art. The court reversed the

Board of Patent Appeals and Interferences' decision and stated: "The factual inquiry whether to combine references must be thorough and searching. It must be based on objective evidence of record. This precedent ... cannot be dispensed with. The need for specificity pervades this authority." The Federal Circuit further stated that omitting the need for a specific suggestion in a particular reference to support the motivation to combine was both a legal error and arbitrary agency action (at 1434). Thus, the generalized motivation to combine fails to rise to the level of particularity required by the Federal Circuit. In the present case, the Examiner has not met the required specificity to establish a motivation to combine the references.

In the absence of some teaching or suggestion in the cited references concerning the method of the present invention, the Examiner has presented no more than an improper hindsight reconstruction of the present invention. As stated by the Court of Appeals for the Federal Circuit *In re Fine*, 5 USPQ2d 1596, 1600 (Fed. Cir. 1988): "One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention." In conclusion, the cited references do not disclose all the limitations of the claims, and there is not motivation to combine the references as suggested by the Examiner. Accordingly, a *prima facie* case of obviousness has not been presented by the Office. Therefore, the Examiner is respectfully requested to withdraw the rejection.

(b) Claim 26 was rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Grossman.

The applicants traverse the rejection. Claim 26 ultimately depends from claim 20, and, therefore, contains all the elements of claim 20. Thus, claim 26 claims an electrophoretic probe having a cleavable linkage L. At no point does Grossman disclose electrophoretic probes having a cleavable linkage L. The cited reference does not disclose all the elements of the claims, and

therefore, a *prima facie* case of obviousness has not been presented by the Office. Therefore, the Examiner is respectfully requested to withdraw the rejection.

(c) Claim 30 was rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Grossman further in view of U.S. Patent No 6,331,530 to Breslow et al. (Breslow).

The applicants traverse the rejection. Breslow is cited to show that singlet oxygen is produced to cleave the linker. In Breslow, two  $\beta$ -cyclodextrin molecules joined by a cleavable linker are cleaved upon exposure to light, and the released molecules are not electrophoretically separated but instead used to kill tumor cells. Breslow does not disclose electrophoretic probes having a cleavable linkage L. As discussed above, Grossman also does not disclose electrophoretic probes having a cleavable linkage L. Thus, the combination of Grossman and Breslow would not provide all the elements of claim 30. Accordingly, a *prima facie* case of obviousness has not been presented by the Office. Therefore, the Examiner is respectfully requested to withdraw the rejection.

#### **Provisional Rejections of the Claims Under Double Patenting**

Claims 21-30 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting over the claims of U.S. Application No. 10/779,255. The applicants will consider filing a terminal disclaimer upon indication of allowable subject matter.

Claims 21-30 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting over the claims of U.S. Patent No. 6,770,439. The applicants will consider filing a terminal disclaimer upon indication of allowable subject matter.

Claims 21-30 were provisionally rejected under the judicially created doctrine of

obviousness-type double patenting over the claims of U.S. Patent No. 7,001,725. The applicants will consider filing a terminal disclaimer upon indication of allowable subject matter.

Claims 21-30 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting over the claims of U.S. Patent No. 6,673,550. The applicants will consider filing a terminal disclaimer upon indication of allowable subject matter.

## **CONCLUSION**

Applicants respectfully submit that the claims define an invention that is patentable over the art, and a notice of allowance is earnestly solicited. If the Examiner has any questions concerning this Response, the Examiner is invited to telephone Applicants' representative at (650) 335-7818.

Respectfully submitted,  
Singh et al.

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